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ORIGINAL ARTICLE

Biomonitoring and risk assessment of organochlorine pesticides among Saudi adults

Nasser Al-Daghri [a,b,*], Sherif H. Abd-Alrahman [a,b,c], Kaiser Wani [a,b], Amaresh Panigrahy [a,b], Philip G. McTernan [d], Omar S. Al-Attas [a,b], Majed S. Alokail [a,b]

[a] *Biomarkers Research Program, King Saud University, PO Box 2455, Riyadh 11451, Saudi Arabia*
[b] *Prince Mutaib Chair for Biomarkers of Osteoporosis, King Saud University, PO Box 2455, Riyadh 11451, Saudi Arabia*
[c] *Pesticides Residues and Environmental Pollution Dept., Central Agricultural Pesticide Laboratory, Agricultural Research Center, Giza 12618, Egypt*
[d] *Department of Biosciences, School of Science and Technology, Nottingham Trent University, NG11 8NS Nottingham, UK*

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Abstract The present study aimed to determine the serum organochlorine pesticides (OCPs) levels and risk of exposure among Saudi adults. Most OCPs are considered as endocrine-disrupting chemicals, and exposure can induce adverse health effects in both humans and wildlife. Serum OCP levels have not been documented in the Saudi population. Serum OCP concentrations were quantified using gas chromatography mass spectrometry (GC-MS/MS) in 302 serum samples collected from adult Saudis. All studied OCPs were detected in all participants. High concentrations of DDT and its metabolites (DDE and DDD) were detected in both males and females, with concentrations being significantly higher in males. High concentrations of 2,4-DDE, 4,4-DDE, and gamma-HCH were detected (18.31, 16.12, and 15.15 ng g^{-1} lipid and 5.9, 7.1, and 8.6 ng g^{-1} lipid for males and females, respectively). Alpha-HCH, Beta-HCH, 2,4-DDT, and 4,4-DDT were detected at concentrations lower than 2 ng g^{-1}. Levels of OCPs varied according to age and body mass index (BMI). Serum concentrations of OCPs significantly differed between Saudi males and females and were influenced by age and BMI. This study is the first to document serum OCP concentrations in Saudi adults from Riyadh, KSA. Monitoring programs are suggested for evaluating serum OCP concentrations in the general population to track toxicity levels and serve as an indicator of possible adverse health effects.

* Corresponding author at: Biochemistry Department, College of Science, King Saud University, PO Box 2455, Riyadh 11451, Saudi Arabia.
E-mail address: aldaghri2011@gmail.com (N. Al-Daghri).
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1. Introduction

Organochlorine pesticides (OCPs) are considered as a group of hazardous substances (ATSDR, 2013), and its classified as persistent organic pollutants (WHO, 2007) due to their lipophilic and bioaccumulation properties (Ali et al., 2016; Carpenter, 2011). Previously, they were widely used in agriculture and industrial applications (Ali et al., 2015). The Stockholm Convention was established in 2001 to phase out these chemicals, which had become a global public health problem (Stockholm Convention, 2009). Human exposure to OCPs is mainly through the consumption of fatty foods (Chung and Chen, 2011) and fish (Batang et al., 2016; Tsukino et al., 2006). Because OCPs are considered endocrine-disrupting chemicals in humans and wildlife (Gregoraszczuk and Ptak, 2013; Meeker, 2012), chronic exposure can lead to serious health effects. OCPs have been documented to be associated with chronic metabolic disorders such as diabetes mellitus type 2 (DMT2) (Al-Othman et al., 2014; Al-Othman et al., 2015b; Codru et al., 2007), reproductive disorders (Bonde, 2010; Hauser et al., 2002; Pflieger-Bruss and Schill, 2000) and neurological problems (Tang et al., 2014; Taylor et al., 2013).

The Kingdom of Saudi Arabia (KSA) has been a signatory of the Stockholm Convention since 2002, but due to weak legislation, there is lack of data on the production and use of these chemicals in the country (Status of ratification, (Stockholm Convention, 2009). Although the industrial use of chemicals in the KSA is limited, exposure through imported consumer products is inevitable (El-Shahawi et al., 2010). Nevertheless, scarce data are available on the presence of these chemicals in KSA (Al-Othman et al., 2015b; Ali et al., 2013a, 2013b; Khan, 2005). Very little information is available in Saudi Arabia, however, with most studies focused only on soil (El-Saeid et al., 2013), water (El Alfy and Faraj, 2017; Magaram, 2009), vegetables (Osman et al., 2010), medicinal plants (Al-Othman et al., 2015a), food contamination (Almutairi, 2013; EL-Saeid, 2010; EL-Saeid and Al-Dosari, 2010), camel's meat (Osman, 2015), municipal solid wastes (El-Saeid et al., 2011; Mohammad, 2009; Osman et al., 2011, 2010) and human milk (Hajjar and Al-Salam, 2016).

This study aimed to determine OCPs levels in blood samples from non-occupational Saudi adults. In the present cross-sectional study, serum concentrations of 10 OCPs [which were identified as being present at the highest levels in our previous published studies (Al-Othman et al., 2014, 2015b)] were measured in adult Saudi volunteers in Riyadh, KSA, to provide information on the serum concentrations of these contaminants in the general Saudi population. Associations between age, gender, BMI, living area, and clinical parameters with OCPs were also investigated.

2. Results and discussion

The data presented in Table 1 summarize the general characteristics of the Saudi adults who participated in the present study. A total of 302 Saudi adults were included, 117 (38.7%) males and 185 (61.3%) females. Out of the 302 adults enrolled in this study, 136 (49%) were diagnosed with DMT2 according to insulin and blood glucose values. The data in the table include age, BMI, hip circumference, waist circumference, systolic-BP, diastolic-BP, cholesterol, HDL-cholesterol, triglycerides, and blood glucose. The results indicated significant differences in BMI, waist circumference, diastolic-BP, HDL, and triglycerides between the male and female participants, whereas no significant differences in hip circumference, systolic-BP, total-cholesterol, or blood glucose were noted.

The results showed a significant differences ($p < 0.01$) in all serum OCPs measured. The detection frequencies (%) of serum OCPs in this study were 22 (alpha-HCH), 34 (beta-HCH), 39 (gamma-HCH), 38.7 (heptachlor), 36.8 (heptachlor-epoxide), 41 (2,4-DDE), 35 (4,4-DDE), 38 (4,4-DDD), 21 (2,4-DDT) and 25 (4,4-DDT) as presented in Fig. 1.

The median serum OCPs concentrations detected in males and females are presented in Fig. 2 the for both observed that 2,4-DDE (18.31–5.86 ng g^{-1} lipid) was the most abundant OCP in serum followed by 4,4-DDE (16.12 – 7.09 ng g^{-1} lipid), gamma-HCH (15.15 – 8.6 ng g^{-1} lipid), heptachlor-epoxide (9.96 – 7.34 ng g^{-1} lipid), 4,4-DDD (7.78 – 5.95 ng g^{-1} lipid), heptachlor (2.77 – 1.87 ng g^{-1} lipid), beta-HCH (1.70 – 1.49 ng g^{-1} lipid), 2,4-DDT (1.42 – 1.39 ng g^{-1} lipid), alpha-HCH (1.27 – 1.40 ng g^{-1} lipid), and 4,4-DDT (1.02 – 0.75 ng g^{-1} lipid), for male and female, respectively.

Recently, three studies observed the relation between OCPs and diabetes among Saudi adults, of which two were our

Table 1 Clinical characteristics of the subjects.

Parameters	Males	Females	P-value
N	117	185	
Age (years)	40.7 ± 7.3	40.4 ± 6.5	0.715
Body Mass Index (kg/m^2)	28.6 ± 3.9	31.6 ± 5.6	0.001
Hip circumference (cm)	106.3 ± 12.6	109.6 ± 12.9	0.087
Waist circumference (cm)	98.9 ± 13.2	95.0 ± 13.0	0.047
Systolic Blood Pressure (mmHg)	117.6 ± 9.7	116.0 ± 11.2	0.266
Diastolic Blood Pressure (mmHg)	77.4 ± 6.9	75.0 ± 7.6	0.013
Glucose (mMol/l)#	7.2 (0.5)	7.0 (0.5)	0.618
Insulin (μU/mL)	14.63 (10.68)	11.84 (10.19)	0.043
Triglycerides (mMol/l)#	1.8 (0.5)	1.6 (0.5)	0.018
Total-Cholesterol (mMol/l)	5.0 ± 1.1	5.1 ± 1.0	0.331
HDL-Cholesterol (mMol/l)	0.78 ± 0.30	0.97 ± 0.34	0.001

Note: Data are presented as the mean ± SD for normal variables, whereas the median (IQR) is used for non-normal variables (#); p-values significant at $p < 0.05$.

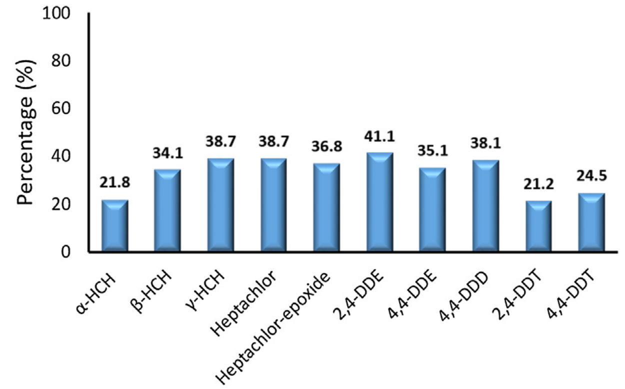

Fig. 1 Mean serum OCP concentrations (ng g^{-1} lipid) for males vs females among all subjects.

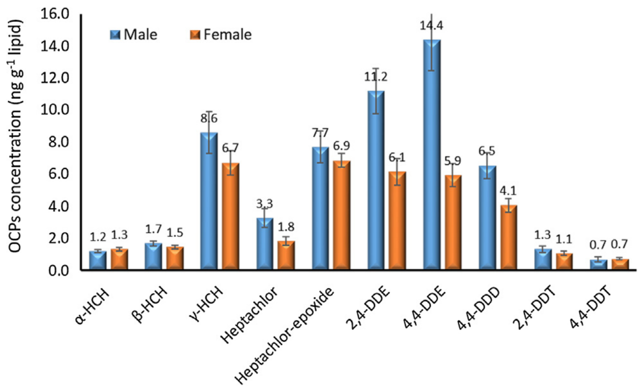

Fig. 2 Frequency percentage of each OCP detected.

previous studies (Al-Othman et al., 2014, 2015b). Their results showed that DMT2 patients have significantly higher concentrations of 2,4-DDE and 4,4-DDE compared to the non-DMT2 subjects and 2,4-DDE had the highest concentration compared to 4,4-DDE and 4,4-DDD in both control and patients, other study by Ali et al. (2016) studied serum OCP levels in DMT2 in Saudi adults from Jeddah and mentioned that OCP levels were higher in DMT2 patients than control. To our knowledge there are no other studies to estimate the serum levels among Saudi population from different areas.

In addition, a comparison between the obtained results of serum OCP levels with previously published studies based on national surveys or monitoring programs conducted on the most environmental pollutants during the last ten years are summarized in Table 2. It is difficult to directly compare these results because the measurements were performed from 2003 to 2012. The median ΣHCH concentration in the present subjects was lower than the median ΣHCH concentration in subjects from China (Hong Kong) (Wang et al., 2013), Tunisia (Ben Hassine et al., 2014), France (Fréry et al., 2011), and South Korea (Son et al., 2010). However, the median ΣHCH concentration in the present subjects was higher than subjects from China (Shanix) (Wang et al., 2014), Japan (Itoh et al., 2009), Pakistan (Ali et al., 2013b), the United Kingdom (Thomas et al., 2006), Italy (Amodio et al., 2012), Belgium (Dirinck et al., 2011), and Canada (Health-Canada, 2010). In addition, the median ΣHCH concentration in the present subjects was lower than the median ΣDDT concentration in subjects from all reported countries.

The present study is one of a very few studies that determined the levels of OCPs in human serum from participants in Riyadh, Saudi Arabia. The obtained results showed that the 10 investigated OCPs: alpha-HCH, beta-HCH, gamma-HCH, heptachlor, heptachlor-epoxide, o,p-DDE, p,p-DDE p,p-DDD, o,p-DDT, and p,p-DDD, were detected in all samples. The frequency of detection (%) for the rest of compounds ranged between 21% and 41%, as shown in Fig. 2. Thus, all studied 10 OCPs were detected, and no individual was free from POPs; the lowest number detected in an individual was two compounds.

Fig. 1 showed significant differences in OCP concentrations between male and female participants. The male participants had significantly higher concentrations of five OCPs than the female participants, including gamma-HCH ($p = 0.024$), heptachlor ($p = 0.003$), o,p-DDE, p,p-DDE, and p,p-DDD (average 55.2% higher in males than in female) ($p \leq 0.001$). Age, sex, and BMI were all statistically significant predictors of serum OCP concentrations. Generally, the OCP serum concentrations tended to increase significantly with age in males, as shown in Fig. 2.

Table 2 Comparison of the median serum levels of OCP congeners (in ng g^{-1} lipid) found in this study and previously reported studies.

Country	Year	N	ΣHCHs	ΣDDTs	ΣOCPs	References
Saudi Arabia (present study)	2016	302	11.37	29.3	40.7	
China (Shanxi)	2010–2012		5.2	64	69.2	Wang et al. (2014)
China (Hong Kong)	2011	54	390	299	689	Wang et al. (2013)
Japan (Nagano Prefecture)	2001–2005	403	0	369.3	369.3	Itoh et al. (2009)
Pakistan (Islamabad)	2012	17	0	162.5	162.5	Ali et al. (2013b)
United Kingdom	2003	154	0	102.9	102.9	Thomas et al. (2006)
Italy (Western Sicily)	2009	101	9.8	179.4	189.2	Amodio et al. (2012)
Tunisia	2012		26.3	193.1	219.4	Ben Hassine et al. (2014)
Belgium	2010		0	205	205	Dirinck et al. (2011)
France	2010		30	124	154	Fréry et al. (2011)
Canada	2009		6.39	167.9	174.3	Health-Canada (2010)
South Korea	2009		57.9	686.5	744.4	Son et al. (2010)
Sudan	2015		92.0	618.0	710.0	Elbashir et al. (2015)
Mexico (Chiapas)	2014		14.99	222.6	237.59	Ruiz-Suarez et al. (2014)

Thus, among the group (age $\leq$ 40 years), significant differences between male and female participants were detected only for p,p-DDE and p,p-DDD ($p = 0.015, 0.037$, respectively). In addition, among the second group (age $\geq$ 40 years), a significant ($p < 0.01$) age-related increase in males for gamma-HCH, heptachlor-epoxide, o,p-DDE, p,p-DDE, and p,p-DDD was found (Figs. 3 and 4). However, female subjects enrolled in this study had significantly higher values for BMI and the lipid profile than the male subjects, but the obtained results showed significantly lower serum OCP levels than males. This finding may be related to the excretion of such compounds by women through lactation, gestation, and the menstrual cycle (Itoh et al., 2009). The differences related to exposure and metabolism between males and females in the general population were not expected, and the factors of lactation and the menstrual cycle can lead to major differences in the levels of organochlorines between males and females, resulting in lower serum concentrations in females (Thomas et al., 2006). A similar gender difference was observed in other studies conducted in Korea, Japan, and Romania. For example, the serum PCB concentrations in subjects living in Seoul in 2001 were significantly different between females and males, and the levels of high chlorinated PCB homologues were particularly higher in males (Park et al., 2007). In Japan, Minh et al. also found significant sex differences for PCB concentrations serum samples taken in Miyako and Saku (Minh et al., 2006).

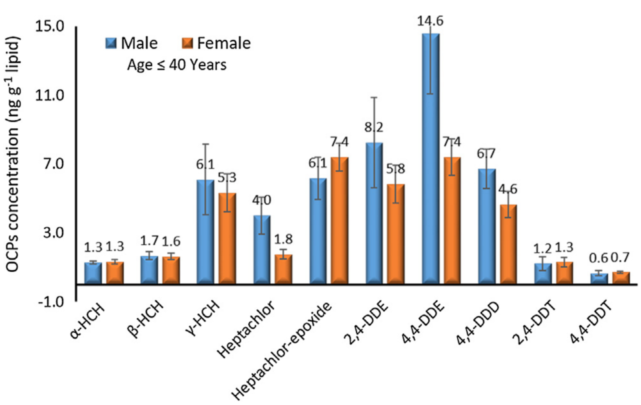

Fig. 3 Mean serum OCP concentrations among males and females with an age less than 40 years old.

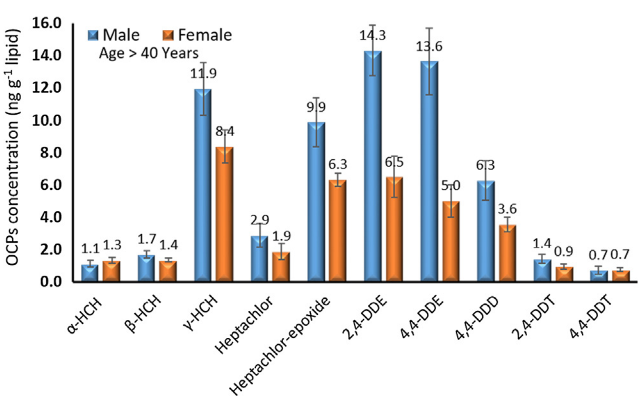

Fig. 4 Mean serum OCP concentrations among males and females with an age more than 40 years old.

In addition, the results obtained from this study suggest that organochlorine chemical levels can be considered as indicators of changes related to human health issues. These results are in agreement with several studies including our previous study on the association between organochlorine concentrations and diabetes, which reported an association between serum DDT and HCH concentrations and the risk of DMT2 in the Saudi population (Al-Othman et al., 2014, 2015b). Longnecker et al. reported that a positive correlation between serum PCBs levels and diabetes among pregnant women in the United States (Longnecker et al., 2001). Lee et al. reported a strong dose-response relationship between OCPs concentration and diabetes, including PCB153, oxychlordane, p,p-DDE, and trans-nonachlor (Lee et al., 2007). In contrast, a different trend of association was reported in the study by Hue et al. (2007), as they reported that there was no relationship between the total plasma organochlorine concentration and BMI; organochlorine concentrations, however, were correlated with age (Hue et al., 2007). The findings related to OCPs reported in both the current and previous studies may help to explain the current worldwide epidemic of metabolic syndrome.

3. Conclusions

To our knowledge, this study is one of the few reports on the distribution of 10 OCP compounds in serum from randomly selected Saudi subjects. Our results showed a positive relationship between the serum concentration of OCPs and sex, with males having higher concentrations than females. In addition, the results indicated that the serum OCP levels increased positively with age. We believe that these results make a considerable contribution to the baseline data on human exposure to OCPs in Saudi Arabia. To improve the knowledge regarding the causes and mechanisms of associated diseases and for public health reasons, further large-scale monitoring studies in the Saudi population are needed, which will clarify POP storage in lipid-rich organs and the relationships between POPs and BMI.

4. Materials and methods

4.1. Study population

Serum samples from 302 adult Saudis (117 males and 185 females), aged 33–48 years old, were randomly selected from Riyadh-wide survey which included all primary care centers, that was initiated by the Biomarkers Research Program (BRP) of King Saud University (KSU) and the Ministry of Health. The inclusion criteria were that the subjects who resident in Riyadh more than 10 years with no occupational exposure to OCPs. Individuals signed the consent form and answered an interviewer-administered structured questionnaire to collect information about their age, gender, place of residence, and medical history information. Ethical approval was obtained from the Ethics Committee of the College of Science Research Center of KSU, Riyadh, Saudi Arabia. Serum samples were stored at −80 °C until analysis.

4.2. Anthropometrics

Anthropometric data; height and weight were measured according to the international standard scale (Digital Person Scale; ADAM Equipment, Milford, CT, USA); waist and hip circumferences were measured using a standard tape measure; and body mass index (BMI), which was calculated as kg/m^2.

4.3. Biochemical parameters

Blood samples were collected during fasting, then centrifuged, and processed on the same day by the assigned primary care physician. Serum was delivered to the Biomarker Research Program (BRP) for initial storage at −20 °C. Serum glucose levels and complete lipid profile ([HDL]-cholesterol, [LDL]-cholesterol, triglycerides and total cholesterol) were measured by a Konelab 20XT biochemical analyzer (Thermo Sc., Finland).

4.4. Sample preparation and standard curve

Extraction of OCPs from human serum was conducted using the liquid-liquid extraction according method of Goni et al. (2007) with slight modification. Briefly, Serum samples, 300 µl each, were put into 2 ml vials then mixed with 500 µl of sodium sulfate 5% water solution and 100 µl of aldrin as internal standard solution containing 50 ng/ml in methanol, were added to serum. Vials, sealed with screw caps, were placed in an ultrasonic bath for 15 min. Sep-Pak C18 cartridges (Waters, USA) were placed on the vacuum manifold and conditioned with 300 µl of methylene-chloride two times, then with 300 µl of methanol and 300 µl of water twice. Samples were loaded onto conditioned cartridges and gentle vacuum was applied. After sample elution, cartridges were rinsed with 500 µl of water twice. Then, C18 cartridges were dried under vacuum for 20 min. The cartridges were eluted with 300 µl of hexane twice and 300 µl of methylene-chloride/hexane (1:1), total, 900 µl were collected into 2 ml glass vials and evaporated using sample-concentrator (CHAIST-AVC 2-25).

A total of 10 OCPs: α-,β-,γ-HCH (hexachlorocyclohexane isomers, expressed here as HCHs), heptachlor, heptachlor-epoxide, 1,1,1-trichloro-2,2-bis (4-chlorophenyl)-ethane (DDT) and DDT metabolite, 1,1-dichloro-2,2-bis(4-chlorophenyl)ethylene (DDE) and 1,1-dichloro-2,2-bis(4-chlorophenyl)ethane (DDD), were analysed in each sample. The standards (purity ≥ 99%) were purchased from Dr. Ehrenstorfer Laboratories (Augsburg, Germany). A stock solution of 10 mixed OCP standards were prepared to containing 10 mg from each in 100 ml n-hexane. A series of mixed OCPs standards, 0.0, 0.5, 2.5, 5, 10, 50, and 100 ng ml^{-1}, was prepared in n-hexane for linearity. Plotting peak area versus concentration was used to generate the Calibration curves for all OCPs presented in this study. The standard calibration curve showed a good linearity, separation and repeatability. The detection limit (LOD) was defined as (signal > 3 times the signal to noise ratio), and the quantification limit (LOQ) was defined as a signal > 10 times the signal to noise ratio. LOD was ranged from 1.2 to 4.0 ng ml^{-1}. The lowest level on the calibration curve was used as the LOQ. A five levels spiked blank matrix samples were used for estimation of the recovery percentage. The serum OCP concentration was normalized by measuring the lipid content as ng/g lipid. The calculation of total lipid (TL, g/l)) was based on the triglycerides (Tg, g/l) and total cholesterol (Tc, g/l) levels according the formula $TL = 0.92 + 1.31 \times (Tg + Tc)$ (Rylander et al., 2006).

4.5. Chromatographic analysis of OCPs

An Agilent 7890 gas chromatograph (GC) was coupled to a 240 series ion trap mass spectrometer (MS) detector. The system was equipped with a DB-5MS capillary column (30 m, 0.25-mm internal diameter, 0.25-mm film). Carrier gas was Helium used at a constant flow (1.0 ml/min). Two microliters of the extract was injected in splitless mode, and the injector temperature was 250 °C. The oven temperature was programmed from 100 °C to 200 °C (hold 2.0 min) at a rate of 15 °C/min and then set to 260 °C at a rate of 5 °C/min. Two ions were monitored for each OCP standards. The standard calibration curve presented excellent linearity with good separation and repeatability. Recovery percentages were calculated from the ratio between the found and expected values and expressed as percentages (%). Recovery percentages were ranged from 86 to 106 %.

4.6. Statistical analysis

Data analyses were performed using SPSS version 22.0 (SPSS Inc., Chicago, Illinois, USA). Data are expressed as the mean ± standard deviation, whereas non-normal data are presented as the geometric mean and coefficient of variation (Cov). The Kolmogorov-Smirnov test was performed to test continuous variables for normality. Independent Student's *t*-test was used to compare means between groups. Non-normal data were log transformed prior to conducting independent sample t-tests. A p-value < 0.05 was considered statistically significant.

4.7. Limitations

There are some limitations in this study. First, this study used 10 OCPs as environmental variables to predict the potential distribution of OCPs in human serum. However, we could not clarify which organochlorine pesticides impacted human health. Second, the sample size was limited, and the number of OCPs measured in the serum samples was limited; thus, further studies are needed to evaluated most of the OCPs that were included in the Stockholm Convention.

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Conflict of interest

The authors declare no conflict of interest.

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